CLAIM

A process for producing f a peptide having a desired biological activity, comprising the steps of:

- (1) culturing cells transformed with an expression vector having the procleotide sequence encoding a peptide of interest that has a helper peptide added thereto, or a fusion protein that has a protective peptide further added to the peptide of interest that has a helper peptide added thereto; and then harvesting said peptide of interest that has a helper peptide added thereto or said fusion protein from said culture;
- (2) in the case wherein a fusion protein is obtained in step (1), cleaving off from said fusion protein the peptide of /interest that has a helper peptide added thereto and the protective peptide, and purifying the peptide of interest that has a helper peptide added thereto as desired;
- (3) in the case wherein modification is required for the peptide of interest, subjecting the peptide of interest that has a helper peptide added thereto obtained in step (1) or step (2) to a modification reaction;
- (4) cleaving off from the peptide of interest that has a helper peptide added thereto obtained in step (1), step (2)/or step (3), the helper peptide and the peptide of interest, and purifying the peptide of interest as desired; and
- (5) purifying the peptide of interest obtained in step (4/)
- The process according to claim 1, wherein said helper peptide has 5 to 50 amino acid residues.
- The process according to claim 1 or 2, wherein said peptide of interest having a helper peptide added thereto has an isoelectric point of 8 to 12.
- The process according to any of claims 1 to 3, wherein said peptide of interest has not more than 200 amino acid residues.

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The process according to any of claims 1 to 4, wherein said protective peptide has 30 to 200 amino acid residues. 6. The process according to 5 wherein an ion exchange resin is used in the purification process. 7. The process according to claim 6, wherein said ion exchange resin is a cation exchange resin. The process according to any wherein a reverse phase chromatography or a hydrophobic 10 chromatography is used in the purification process. The process according to an م wherein a surfactant and/or a salt are added in at least one of steps (1) to (5) to maintain the solubility of the 15 peptide of interest. The process according to an C wherein the host cell is a prokaryotic cell or a eukaryotic cell. 11. The process according to claim 10, wherein the 20 host cell is Escherichia coli. 12. The process according to any of claims 1 to T1, a wherein the isoelectric point of the peptide of interest having a helper peptide added thereto, is 8 to 12. The process according to any of wherein the peptide of interest is an amidated peptide. 25 The process according to any a wherein the peptide of interest is a GLP-1 derivative having an insulinotropic activity. The process according to claim 14, wherein the 30 GLP-1 derivative having an insulinotropic activity that has a helper peptide added thereto has an isoelectric point of 8 to 12. The process according to claim 14 or 15, a wherein the GLP-1 derivative having an insulinotropic 35 activity has an isoelectric point of 4.5 to 9.0. The process according to claim 14 or 15,

wherein the GLP-1 derivative having an insulinotropic

activity has an isoelectric point of 5.5 to 7.5.

- 18. The process according to any of claims 12 to 17, wherein an ion exchange resin is used in the purification process.
 - 19. The process according to claim 18, wherein said ion exchange resin is a cation exchange resin.
 - 20. The process according to any of claims 12 to 17, wherein a reverse phase chromatography or a hydrophobic chromatography is used in the purification process.
 - 21. The process according to any of claims 12 to 477 wherein a surfactant and/or a salt is added to maintain the solubility of the peptide of interest.
 - 22. The process according to any of claims 14 to 21, wherein the purity of the GLP-1 derivative obtained having an insulinotropic activity is 98% or greater.
 - 23. The process according to any of claims 1 to 22 wherein the content of endotoxin in the final purified product is not greater than 0.03 units/mg.
 - 24. A pharmaceutical composition for treatment of diabetes mellitus comprising as an active ingredient a GLP-1 derivative having an insulinotropic activity, obtained from the process according to any of claims 14-20-23.
 - 25. An expression vector comprising a nucleotide sequence encoding a peptide of interest that has a helper peptide added thereto, or a fusion protein that has a protective peptide further added to the peptide of interest that has a helper peptide added thereto.
 - 26. A prokaryotic or a eukaryotic cell transformed with an expression vector comprising a nucleotide sequence encoding a peptide of interest that has a helper peptide added thereto, or a fusion protein that has a protective peptide further added to the peptide of interest that has a helper peptide added thereto.
 - 27. The cell according to claim 26, wherein the host cell is <u>Escherichia coli</u>.

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